

# Exhibit 4

UNITED STATES DISTRICT COURT  
CENTRAL DISTRICT OF CALIFORNIA

ALLERGAN USA, INC., and  
ALLERGAN INDUSTRIE, SAS,

Plaintiffs,

v.

MEDICIS AESTHETICS, INC., MEDICIS  
PHARMACEUTICAL CORP., VALEANT  
PHARMACEUTICALS NORTH AMERICA LLC,  
VALEANT PHARMACEUTICALS  
INTERNATIONAL, VALEANT  
PHARMACEUTICALS INTERNATIONAL, INC.,  
and GALDERMA LABORATORIES, L.P.

Defendants.

Case No. 8:13-cv-01436 AG (JPRx)

**REPORT OF GLENN D. PRESTWICH, Ph.D.**

**FEBRUARY 17, 2015**

**CONFIDENTIAL MATERIAL SUBJECT TO PROTECTIVE ORDER**

Puragen<sup>®</sup> Plus and Prevelle Silk also contain uncrosslinked HA, i.e., 6% and 2%, respectively. As discussed in Section VII.A, although the HA products crosslinked with DEO, BCDI and DVS are chemically distinct and different from the HA-BDDE products, all produced stable and sterile soft tissue fillers when combined with lidocaine. This indicates or strongly suggests that sterile and stable soft tissue fillers containing lidocaine, crosslinked HA in general regardless of the type of crosslinker, with or without uncrosslinked HA, can be obtained using methods known in the art. I am not aware of any teaching in the prior art that suggests that lidocaine would cause a stable soft tissue filler containing uncrosslinked HA and HA-BDDE to be unstable, when it was known that the filler containing uncrosslinked HA and HA-BDDE is stable, and it was further known that fillers containing lidocaine and three other types of crosslinked HA, with or without uncrosslinked HA, are also stable.

144. The claim construction and definition as found in the patents require that only a single property – one of which includes sterility – remain constant. Additionally, the definition of stability sets forth no specific reference period over which this “stability” must be maintained. The patent specifications do refer to a two-month time period,<sup>132</sup> but I have been informed by counsel for Defendants that Plaintiffs have affirmatively rejected any minimum required time period during claim construction in this case.

145. Moreover, claims 1, 3, 8, and 11 of the ‘795 Patent do not have a stability claim term applied to the claimed soft tissue filler. Even assuming that the inventor’s contentions about stability were true, a POSITA would have a reasonable expectation of success to obtain the claimed sterile composition by simply adding lidocaine to a pre-existing Juvederm product, then sterilizing the mixture using “any method known in the art to effectively kill or eliminate

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<sup>132</sup> ‘475 Patent, 8:6-8.

transmissible agents”<sup>133</sup>, or by simply mixing a sterile lidocaine solution with a sterile HA composition as done routinely by practitioners in clinics.<sup>134</sup>

**B. The percentage of uncrosslinked HA does not make the claims patentable**

146. Some claims of the patents-in-suit recite a level of uncrosslinked HA exceeding about 10% uncrosslinked HA. I was asked to opine on whether the claimed amount of uncrosslinked HA would have made the claimed fillers patentable over the prior art.

147. In my opinion, the claimed amount of uncrosslinked HA would not have made the claimed filler compositions patentable over the prior art, at least because the claimed amount of uncrosslinked HA was either already used in the prior art or would have been easily obtained by routine experimentation. As I discussed above in Section VII.A.7, uncrosslinked HA is included in the filler mainly as a lubricant to ease the injection of crosslinked HA. It was known to a POSITA that a larger amount of uncrosslinked HA is needed when more extrusion force is required to inject the crosslinked HA, such as crosslinked HA with higher viscosity, higher degree of crosslinking, larger particle sizes, etc. However, when all other relevant parameters are identical, the higher percentage of uncrosslinked HA in an HA gel, the faster the HA gel may be degraded and be resorbed *in vivo*. It is within routine experimentation for a POSITA to choose the appropriate percentage of uncrosslinked HA that achieves the lubricant function without sacrificing the desired persistence of the filler product.

148. Stable, sterile soft tissue fillers containing at least 10% uncrosslinked HA and HA-BDDE were already taught by the prior art. For example, the composition described in Example 2 of *Debacker* contains HA-BDDE and uncrosslinked HA mixed at a ratio of 2:1 (thus

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<sup>133</sup> ‘795 Patent, 12:4-5.

<sup>134</sup> See *Beasley*, p. 92.

180. For these reasons, the asserted claims of the '475 Patent are obvious in light of the disclosures in *Hunter*, *Sadozai*, and *Reinmuller II*.

181. Element-by-element charts for these can be found at Exhibit D..

2. *Previously Known Pre-mixing of Lidocaine and Restylane/Perlane/Juvederm Product*

182. Additionally, as noted above in paragraph 145, I have been told that practitioners were mixing lidocaine and HA-BDDE dermal fillers using connectors before injection of the dermal filler from the period shortly after the HA-BDDE fillers were approved and available on the market.

183. As noted above in Paragraphs 169 and 170, Allergan asserts that Restylane-L and Perlane-L practice all elements of the asserted claims of the '475 Patent, while their asserted Juvederm XC products practice select claims of the '475 Patent. As I note in paragraph 169, the only difference between these products and the same brand names without lidocaine is the lidocaine.

184. Once the lidocaine had been added, I have been told that practitioners would inject the sterile substance into their patients as they would with any dermal filler. I have been told that the product remained sterile and clinically useful before injection took place.

185. The successful practice of adding lidocaine to HA dermal fillers would make it obvious to a POSITA that adding lidocaine during the manufacturing process was able to be done and could result in a final, lidocaine-containing dermal filler that had the elements of the asserted claims in view of the common knowledge in the art about HA fillers and lidocaine such as that described in this report. Variations on degree of crosslinking, concentration of lidocaine, and amount of free HA had all been disclosed in the prior art and would all be obtainable through experimentation.

186. For the foregoing reasons, the asserted claims of the '475 Patent would have been obvious in light of the pre-mixing of lidocaine with crosslinked HA dermal fillers of the Restylane and Juvederm families performed by practitioners in view of the common knowledge.

3. *Debacker*

187. *Debacker* discloses and describes compositions comprised of an insoluble hydrogel of a crosslinked polymer contained within an aqueous solution of the polymer.<sup>179</sup> More specifically, *Debacker* concerns a dermal filler of HA-BDDE in uncrosslinked HA at a 2-to-1 ratio.<sup>180</sup> *Debacker* also teaches the packaging and autoclave sterilization of this filler.<sup>181</sup>

188. Element-by-element charts for *Debacker* can be found in Exhibit D.

a. In combination with *Sadozai*

189. *Sadozai* teaches an HA-BCDI composition for use in tissue augmentation.<sup>182</sup> More than this teaching, however, *Sadozai* also teaches that lidocaine can have a “synergistic effect” on the rheological properties of crosslinked HA and provide stabilization during and following autoclave sterilization.<sup>183</sup>

190. For the general reasons discussed above in Section VIII.A, a POSITA would have been highly motivated to modify the explicitly disclosed filler in *Debacker* to include lidocaine. This is particularly true in view of *Sadozai*, given the pain relief possibilities and potential synergies created by adding lidocaine to such a composition.

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<sup>179</sup> *Debacker*, 3:15-19.

<sup>180</sup> *Id.*, Example 2.

<sup>181</sup> *Id.*, 14:22-24.

<sup>182</sup> *Sadozai*, Abstract.

<sup>183</sup> *Id.*, Example 21; Fig. 7; paras. [0068] and [0069].

225. As noted above in Paragraph 222, *Wang* uses examples wherein HA is crosslinked with BDDE.<sup>210</sup> This addresses the additional claim element found in the asserted Claim 8.

226. For the foregoing reasons, *Wang* anticipates claims 1, 3, and 8 of the '795 Patent.

2. *Previously Known Pre-mixing of Lidocaine and Restylane/Perlane/Juvederm Product*

227. Additionally, as noted above in paragraph 145, I have been told that practitioners were mixing lidocaine and HA-BDDE dermal fillers using connectors before injection of the dermal filler from the period shortly after the HA-BDDE fillers were approved and available on the market.

228. As noted above in Paragraphs 169 and 170, Allergan asserts that Restylane-L and Perlane-L practice all elements of the asserted claims of the '795 Patent, while their asserted Juvederm XC products practice select claims of the '795 Patent. As I note in paragraph 169, the only difference between these products and the same brand names without lidocaine is the lidocaine.

229. Once the lidocaine had been added, I have been told that practitioners would inject the sterile substance into their patients as they would with any dermal filler. I have been told that the product remained sterile and clinically useful before injection took place.

230. Claims 1, 3, 8, and 41 have no requirements for particular concentrations of crosslinked HA, free HA, or lidocaine. For the foregoing reasons, the pre-mixing of lidocaine with crosslinked HA dermal fillers of the Restylane and Juvederm families would anticipate the asserted claims of the '795 Patent.

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<sup>210</sup> *Wang*, Examples 1-7.

234. For these reasons, the asserted claims are obvious in light of the disclosures in *Hunter, Sadozai, Reinmuller II*, and *Wang*.

2. *Previously Known Pre-mixing of Lidocaine and Restylane/Perlane/Juvederm Product*

235. Additionally, as noted above in paragraph 145, I have been told that practitioners were mixing lidocaine and HA-BDDE dermal fillers using connectors before injection of the dermal filler from the period shortly after the HA-BDDE fillers were approved and available on the market.

236. The successful practice of adding lidocaine to HA dermal fillers would make it obvious to a POSITA that adding lidocaine during the manufacturing process was able to be done and could result in a final, lidocaine-containing dermal filler that had the elements of the asserted claims in view of the common knowledge in the art about HA fillers and lidocaine such as that described in this report. Variations on degree of crosslinking, concentration of lidocaine, and amount of free HA had all been disclosed in the prior art and would all be obtainable through experimentation.

237. For the foregoing reasons, the asserted claims of the '795 Patent would be obvious in light of the pre-mixing of lidocaine with crosslinked HA dermal fillers of the Restylane and Juvederm families performed by practitioners.

3. *Expert Anti-Aging in view of Toth*

238. *Expert Anti-Aging* discloses VOLUMA Corneal<sup>®</sup> (Juvederm<sup>®</sup> Voluma), which has the identical specifications of Juvederm<sup>®</sup> Voluma XC except for the inclusion of 0.3% (w/w) lidocaine in the XC product.<sup>212</sup>

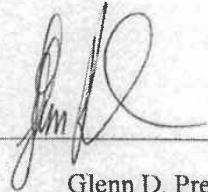
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<sup>212</sup> *Juvederm FDA Briefing*, pp. 20-21.



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Executed this 17<sup>th</sup> day of February, 2015.

  
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Glenn D. Prestwich, Ph.D.

## **Exhibit D**

*Pre-mixing by Practitioners:*

The '475 patent	Prior Art Evidencing Obviousness of '475 Patent Claims
<b>Claim 1</b>	
A stable, sterile soft tissue filler comprising: paragraph	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 1 of the '475 patent, then this element was already known in the art.
a hyaluronic acid (HA) component comprising HA crosslinked with 1,4-butanediol diglycidyl ether (BDDE), and	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 1 of the '475 patent, then this element was already known in the art.
uncrosslinked HA, wherein the HA component comprises greater than about 10% uncrosslinked HA by volume; and	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 1 of the '475 patent, then this element was already known in the art.
lidocaine combined with said crosslinked HA component.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 1 of the '475 patent, then this element was already known in the art.
<b>Claim 2</b>	
The soft tissue filler of claim 1 wherein the HA component comprises at least about 15% uncrosslinked HA by volume.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 2 of the '475 patent, then this element was already known in the art.
<b>Claim 4</b>	
The soft tissue filler of claim 1 wherein the HA component comprises a first portion of crosslinked HA and a second portion of uncrosslinked HA.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 4 of the '475 patent, then this element was already known in the art.



<b>Claim 5</b>	
The soft tissue filler of claim 4 wherein the first portion has degree of crosslinking of less than about 6%.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 5 of the '475 patent, then this element was already known in the art.
<b>Claim 6</b>	
The soft tissue filler of claim 4 wherein the HA component has a degree of crosslinking of less than about 5%.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 6 of the '475 patent, then this element was already known in the art.
<b>Claim 8</b>	
The soft tissue filler of claim 1 wherein the lidocaine is at a concentration of between about 0.1% and about 5% by weight of said soft tissue filler.	To the extent the lidocaine added by practitioners did not fall within the claimed range, multiple resources pointed to lidocaine concentrations in the ranges covered by the claim element. <i>See, e.g., Toth</i> (“a stable formulation of cross linked HA (28 mg/ml) and lidocaine (0.3%) was developed”; <i>Sadozai</i> , paragraph [0068] (“...the composition is stabilized, by the inclusion of a local anesthetic, e.g., lidocaine”; <i>Sadozai</i> , example 21 (“Crosslinked HA of Example 5 was processed as in Example 12 using three separate buffers 1 (no lidocaine), 2 (0.2% lidocaine), and 3 (0.3% lidocaine).”); <i>Reinmuller 1</i> , 7:1-15.
<b>Claim 9</b>	
The soft tissue filler of claim 1 wherein the HA component comprises particles of crosslinked HA in a relatively fluidic medium of uncrosslinked HA.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 9 of the '475 patent, then this element was already known in the art.
<b>Claim 18</b>	
A stable, sterile soft tissue filler comprising:	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 18 of the '475 patent, then this element was already known in the art.
a hyaluronic acid (HA) component crosslinked with 1,4-butanediol diglycidyl ether (BDDE),	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 18 of the '475 patent, then this element was already known in the art.

said HA component having a degree of crosslinking of less than about 5% and	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 18 of the '475 patent, then this element was already known in the art.
uncrosslinked HA in an amount of at least about 10% by volume of the HA component; and	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 18 of the '475 patent, then this element was already known in the art.
lidocaine having a concentration of about 0.3% by weight of said soft tissue filler;	To the extent the lidocaine used by practitioners did not fall within this claimed range, multiple resources pointed to lidocaine concentrations in the ranges covered by the claim element. <i>See, e.g., Toth</i> ("a stable formulation of cross linked HA (28 mg/ml) and lidocaine (0.3%) was developed"; <i>Sadozai</i> , paragraph [0068] ("...the composition is stabilized, by the inclusion of a local anesthetic, e.g., lidocaine"; <i>Sadozai</i> , example 21 ("Crosslinked HA of Example 5 was processed as in Example 12 using three separate buffers 1 (no lidocaine), 2 (0.2% lidocaine), and 3 (0.3% lidocaine)."); <i>Reinmuller 1</i> , 7:1-15.
wherein the soft tissue filler has been heat sterilized.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 18 of the '475 patent, then this element was already known in the art.
<b>Claim 31</b>	
A heat-sterilized, stable dermal filler comprising:	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 31 of the '475 patent, then this element was already known in the art.
a hyaluronic acid (HA) comprising both crosslinked HA and uncrosslinked HA,	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 31 of the '475 patent, then this element was already known in the art.
the crosslinked HA being crosslinked with 1,4-butanediol diglycidyl ether (BDDE) and	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 31 of the '475 patent, then this element was already known in the art.
having a degree of crosslinking of less than about 5%; and	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 31 of the '475 patent, then this element was already known in the art.

lidocaine at a concentration of about 0.3% by weight of said dermal filler;	To the extent the lidocaine added by practitioners did not fall within this claimed range, multiple resources pointed to lidocaine concentrations in the ranges covered by the claim element. <i>See, e.g., Toth</i> (“a stable formulation of cross linked HA (28 mg/ml) and lidocaine (0.3%) was developed”; <i>Sadozai</i> , paragraph [0068] (“...the composition is stabilized, by the inclusion of a local anesthetic, e.g., lidocaine”; <i>Sadozai</i> , example 21 (“Crosslinked HA of Example 5 was processed as in Example 12 using three separate buffers 1 (no lidocaine), 2 (0.2% lidocaine), and 3 (0.3% lidocaine).”); <i>Reinmuller 1</i> , 7:1-15.
the dermal filler having a pH of about 7.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 31 of the ‘475 patent, then this element was already known in the art.
<b>Claim 32</b>	
The dermal filler of claim 31 having a HA concentration of between about 20 mg/mL to about 30 mg/mL.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 32 of the ‘475 patent, then this element was already known in the art.



<b>Claim 33</b>	
The dermal filler of claim 31 wherein the HA comprises at least about 10% to about 20% of the uncrosslinked HA by volume.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 33 of the '475 patent, then this element was already known in the art.
<b>Claim 34</b>	
A stable, sterile soft tissue filler comprising:	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 34 of the '475 patent, then this element was already known in the art.
a hyaluronic acid (HA) component comprising HA crosslinked with 1,4- butanediol diglycidyl ether (BDDE), and uncrosslinked HA; and	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 34 of the '475 patent, then this element was already known in the art.
lidocaine at a concentration of about 0.3% by weight of the soft tissue filler combined with said crosslinked HA component;	To the extent the lidocaine added by practitioners was not within this claimed range, multiple resources pointed to lidocaine concentrations in the ranges covered by the claim element. <i>See, e.g., Toth</i> ("a stable formulation of cross linked HA (28 mg/ml) and lidocaine (0.3%) was developed"; <i>Sadozai</i> , paragraph [0068] ("...the composition is stabilized, by the inclusion of a local anesthetic, e.g., lidocaine"; <i>Sadozai</i> , example 21 ("Crosslinked HA of Example 5 was processed as in Example 12 using three separate buffers 1 (no lidocaine), 2 (0.2% lidocaine), and 3 (0.3% lidocaine)."); <i>Reinmuller 1</i> , 7:1-15.
wherein the soft tissue filler is stable after heat sterilization at between about 120 degrees C. and about 130 degrees C.; and	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 34 of the '475 patent, then this element was already known in the art.
wherein the soft tissue filler has a pH of about 7.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. This product would inherently be controlled to about 7 to allow for injection into the human body. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 34 of the '475 patent, then this element was already known in the art.
<b>Claim 35</b>	

The soft tissue filler of claim 34 having a HA concentration of between about 20 mg/mL to about 30 mg/mL.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 35 of the '475 patent, then this element was already known in the art.
<b>Claim 36</b>	
The soft tissue filler of claim 34 wherein the HA comprises at least about 10% to about 20% of the uncrosslinked HA by volume.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 36 of the '475 patent, then this element was already known in the art.
<b>Claim 37</b>	
The soft tissue filler of claim 34 wherein the crosslinked HA has a degree of crosslinking of less than about 5%.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 37 of the '475 patent, then this element was already known in the art.



## **Exhibit E**

*Pre-mixing by Practitioners:*

The '795 patent	Prior Art Evidencing Anticipation of '795 Patent
<p><b>Claim 1</b></p> <p>A soft tissue filler composition comprising: a hyaluronic acid (HA) component crosslinked with a crosslinking agent selected from the group consisting of 1,4-butanediol diglycidyl ether (BDDE ), 1,4-bis(2,3-epoxypropoxy)butane, 1,4-bisglycidylloxybutane, 1,2-bis(2,3-epoxypropoxy)ethylene and 1-(2,3-epoxypropyl)-2,3-epoxycyclohexane, and 1,4-butanediol diglycidyl ether;wherein the HA is not crosslinked to a non-HA biopolymer; and lidocaine combined with said crosslinked HA component; wherein the lidocaine is freely released in vivo; and wherein the composition is sterile.</p>	<p>Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 1 of the '795 patent, then claim 1 is anticipated by the pre-mixing performed by practitioners.</p>
<p><b>Claim 3</b></p>	

The soft tissue filler composition of claim 1 wherein the HA component is a hydrated gel.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 3 of the '795 patent, then claim 3 is anticipated by the pre-mixing performed by practitioners.
<b>Claim 8</b>	
The soft tissue filler composition of claim 1 wherein the crosslinking agent is BDDE.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 8 of the '795 patent, then claim 8 is anticipated by the pre-mixing performed by practitioners.

**Exhibit F**

*Pre-mixing by Practitioners:*

The '795 patent	Prior Art Evidencing Obviousness of '795 Patent Claims
<b>Claim 1</b>	
A soft tissue filler composition comprising:	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 1 of the '795 patent, then this element was already known in the art.
a hyaluronic acid (HA) component crosslinked with a crosslinking agent selected from the group consisting of 1,4-butanediol diglycidyl ether (BDDE ), 1,4-bis(2,3-epoxypropoxy)butane, 1,4-bisglycidyl ether, 1,2-bis(2,3-epoxypropoxy)ethylene and 1-(2,3-epoxypropyl)-2,3-epoxycyclohexane, and 1,4-butanediol diglycidyl ether;	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 1 of the '795 patent, then this element was already known in the art.
wherein the HA is not crosslinked to a non-HA biopolymer; and	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 1 of the '795 patent, then this element was already known in the art.

lidocaine combined with said crosslinked HA component;	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 1 of the '795 patent, then this element was already known in the art.
wherein the lidocaine is freely released in vivo; and	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. This lidocaine was pre-mixed in order to relieve pain immediately. In order for the lidocaine to fulfill its medicinal purpose, it must be able to release from the gel.
wherein the composition is sterile.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 1 of the '795 patent, then this element was already known in the art.
<b>Claim 3</b>	
The soft tissue filler composition of claim 1 wherein the HA component is a hydrated gel.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 3 of the '795 patent, then this element was already known in the art.
<b>Claim 8</b>	
The soft tissue filler composition of claim 1 wherein the crosslinking agent is BDDE.	Practitioners would premix HA-BDDE dermal fillers such as Restylane® and the early Juvederm products with lidocaine. The practitioner would then inject the dermal filler into a patient. As Restylane-L® is merely the earlier Restylane® compound with the addition of lidocaine, and as Restylane-L® is alleged by Allergan to infringe claim 8 of the '795 patent, then this element was already known in the art.
<b>Claim 11</b>	

<p>The soft tissue filler composition of claim 1 wherein the lidocaine is present at a concentration between about 0.1% and about 5.0% by weight of said composition.</p>	<p>To the extent the lidocaine used by practitioners did not fall within the asserted range, multiple resources pointed to lidocaine concentrations in the ranges covered by the claim element. <i>See, e.g., Toth</i> (“a stable formulation of cross linked HA (28 mg/ml) and lidocaine (0.3%) was developed”; <i>Sadozai</i>, paragraph [0068] (“...the composition is stabilized, by the inclusion of a local anesthetic, e.g., lidocaine”; <i>Sadozai</i>, example 21 (“Crosslinked HA of Example 5 was processed as in Example 12 using three separate buffers 1 (no lidocaine), 2 (0.2% lidocaine), and 3 (0.3% lidocaine).”); <i>Reinmuller 1</i>, 7:1-15.</p>
<p><b>Claim 41</b></p>	
<p>The composition of claim 1, wherein the composition has an extrusion force that is substantially constant for at least 9 months.</p>	<p>Extrusion force is an inherent property of the composition. Extrusion force is also a matter of routine experimentation for a commercial product.</p>